# Cardiovascular burden prior to diagnosis of hereditary transthyretin amyloidosis

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### **BACKGROUND/INTRODUCTION**

- Hereditary transthyretin (ATTRv or hATTR) amyloidosis is a protein folding disorder often associated with cardiac involvement<sup>1,2</sup>
- Cardiac involvement in ATTRv is associated with poor survival<sup>1,3,4</sup> • Patients often have long-standing cardiac symptoms prior to their amyloidosis diagnosis, and it has been shown that diagnostic delay can result in increased
- disease burden and progressive myocardial injury and failure<sup>1,3</sup> • Real-world evidence focusing on cardiac manifestations throughout the ATTRv patient journey is limited<sup>1,3</sup>

### PURPOSE

• To examine the presence of cardiovascular manifestations among patients with ATTRv amyloidosis, in the years leading up to diagnosis.

### METHODS

### Study design and data source

 Retrospective claims analysis of IBM<sup>®</sup> MarketScan<sup>®</sup> Commercial and Medicare Supplemental\* data (US) from 1/1/2011-12/31/2017

### **Patient identification**

Inclusion criteria

- Adult patients (≥18 years of age) newly diagnosed with ATTRv amyloidosis identified using a claims-based algorithm as follows:
- At least 1 medical claim with relevant amyloidosis diagnosis code (ICD-10-CM: E85.0-.4, E85.89, E85.9; excluding light chain and wild type) during identification (ID) period of 1/1/16-12/31/17, and the occurrence of  $\geq 1$  qualifying criteria during any time in study period:
- $\geq 15$  days diflurisal use without > 30-day gap OR liver transplantation
- Patients with specific claim codes E85.1 (neuropathic heredofamilial amyloidosis) or E85.2 (heredofamilial amyloidosis, unspecified) at any time did not require additional qualifier
- Study index date was defined as the date of first claim with an amyloidosis diagnosis in ID period
- A look-back period during the 5 years prior to the index date was used to examine cardiovascular manifestations leading up to diagnosis
- Patients had continuous health plan enrollment during the look-back period

### **Exclusion criteria**

• To ensure that only patients with a new diagnosis were included, those with an ICD-9/10 amyloidosis code during the look-back period were excluded

### **Disease-free control group**

- To serve as a reference group, an ATTRv-free cohort was created including patients without ATTRv diagnosis and matched 3:1 to ATTRv patients based upon age, gender, and region
- The same index and enrollment requirements as ATTRv patients were used for matched patients

### Study measures

- Frequency of selected cardiovascular conditions (hypotension, aortic stenosis, congestive heart failure, dyspnea, edema, stroke (ischemic, hemorrhagic), bleeding, hypertrophic cardiomyopathy, restrictive cardiomyopathy, ventricular hypertrophy, atrial fibrillation/flutter, syncope, chest pain, bradycardia) during the 5-year look-back period
- Frequency of diagnostic testing (blood/urine testing and cardiac imaging (i.e., pyrophosphate imaging, cardiac MRI, and echocardiogram)), hospitalization, and emergency department (ED) visits were determined during the 5-year look-back period
- Demographics and Charlson comorbidity index (CCI) were determined 1 year prior to or on the index date

### Statistical analysis

- Descriptive statistics generated for pre-index measures during each year of look-back period
- The cumulative probability of occurrence of selected comorbidities and diagnostic testing since 5 years before the index date was generated

\*MarketScan is a trademark of IBM Corporation in the United States and other countries.

### RESULTS

### Baseline demographics and comorbidities during the 1-year pre-index period (Table 1)

## pre-index period

## Age, year, mea

- 18-34, n (%)
- 35-54
- 55-64

65+

- Female, n (%)
- Region, n (%)
- Midwest
- Northeast
- South
- West

Insurance type,

- PPO/POS
- HMO/EPO
- CDHP/HDHP
- Comprehensiv
- Charlson como
- Number of chror
- Usual physicia
- Primary Care
- Cardiologist
- Dermatologis
- Gastroenter
- Neurologis
- Rheumatolog
- Other<sup>c</sup>/Unkno

<sup>a</sup>Matched with age, gender, and region. <sup>b</sup>Two matched controls had missing/unknown insurance type. °Includes podiatrists and individual specialties with count <5.</p>

• Among 141 patients with ATTRv and 423 matched controls meeting inclusion criteria, mean (SD) age was 62.5 (14.2) years, with the majority (76%) having a diagnosis at age 55 years or older, and 53.9% were female

• Mean CCI for ATTRv patients was 2.7 (3.0) vs 1.1 (1.9) for matched controls 
 Table 1. Baseline demographic and comorbidities during 1-year

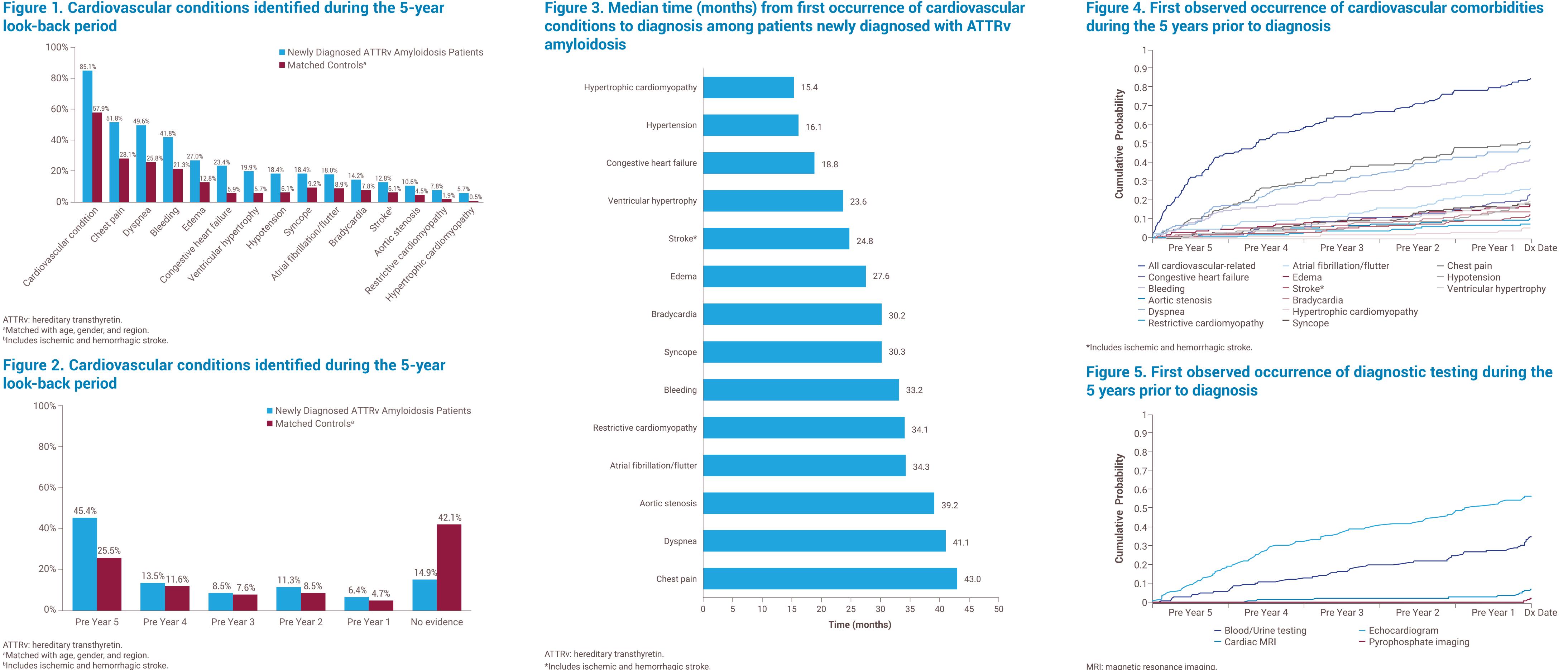
Ja		
	Newly Diagnosed ATTRv Amyloidosis Patients N=141	Matched Controls <sup>a</sup> N=423
n (SD)	62.5 (14.3)	62.5 (14.2)
	6 (4.3)	18 (4.3)
	27 (19.1)	81 (19.1)
	52 (36.9)	156 (36.9)
	56 (39.7)	168 (39.7)
	76 (53.9)	228 (53.9)
	26 (18.4)	78 (18.4)
	47 (33.3)	141 (33.3)
	55 (39.0)	165 (39.0)
	13 (9.2)	39 (9.2)
e, n (%) <sup>b</sup>		
	99 (70.2)	239 (56.5)
	8 (5.7)	30 (7.1)
	14 (9.9)	72 (17.0)
ive	20 (14.2)	80 (18.9)
orbidity index, mean (SD)	2.7 (3.0)	1.1 (1.9)
onic conditions, mean (SD)	5.1 (2.7)	3.2 (2.3)
n specialty, n (%)		
)	65 (46.1)	230 (54.4)
	5 (3.5)	10 (2.4)
st	4 (2.8)	16 (3.8)
ologist	6 (4.3)	6 (1.4)
	6 (4.3)	2 (0.5)
gist	5 (3.5)	6 (1.4)
own	50 (35.5)	153 (36.2)
vretin: CDHP/HDHP: consumer directed health	valere / bigh deductible beelth slave FDC	

ATTRv: hereditary transthyretin; CDHP/HDHP: consumer directed health plan/high deductible health plan; EPO: exclusive provider organization; HMO: health maintenance organization; PPO/POS: preferred provider organizations/point of service.

### Healthcare utilization and cardiovascular comorbidities during the 5-year look-back period

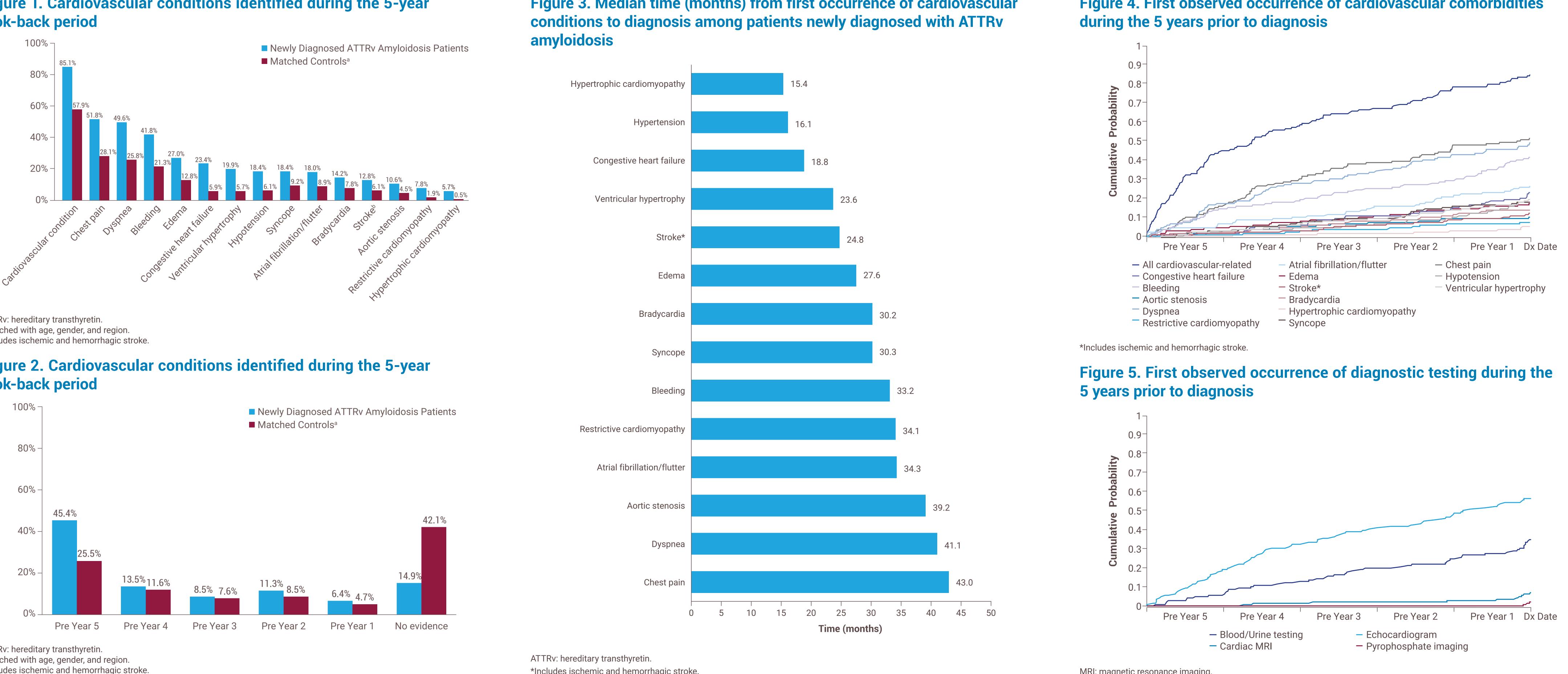
- a few patients (**Figure 5**)

## look-back period



<sup>a</sup>Matched with age, gender, and region.

## look-back period



ATTRv: hereditary transthyretin.

<sup>b</sup>Includes ischemic and hemorrhagic stroke.

### CONCLUSIONS

- This study has potential limitations:

### REFERENCES

DISCLOSURES

Company Relationship; Akcea Therapeutics. J.T. Ortiz-Pérez: Speaker's Bureau; Company Relationship; General Electric, Akcea Therapeutics SL, Medical Dosplus SL, AstraZeneca SL, Bristol-Myers Squibb-Pfizer, Psyma Iberica Marketing Research M. Vera-Llonch: Employee: C Board Membership; Company Relationship; Akcea Therapeutics. **B.R. Reddy:** Consultant; Company Relationship; Akcea Therapeutics. **E. Chang:** Consultant; Company Relationship; Company Relationship; Akcea Therapeutics. **E. Chang:** Consultant; Company Relationship; Akcea Therapeutics. **E. Chang:** Consultant; Company Relationship; Company Relationship; Company Relationship; Company Relationship; Co Stock or Stock Options; Company Relationship; Akcea Therapeutics, Alnylam Pharmaceuticals, Pfizer, Eidos Therapeutics, Eidos Therapeutics, Alnylam Pharmaceuticals, Pfizer, Eidos Therapeutics, Pfizer, Eidos Therapeutics, Pfizer, Eidos Therapeuti Support; Company Relationship; Akcea Therapeutics, Pfizer, Alnylam Pharmaceuticals. Consultant; Company Relationship; Akcea Therapeutics, Pfizer, Alnylam Pharmaceuticals.

• Cardiovascular manifestations were common among ATTRv patients prior to diagnosis

- A higher proportion of ATTRv patients vs. matched controls had each cardiovascular condition during the look-back period (Figure 1)

- Cardiovascular conditions were relatively higher for ATTRv patients vs. matched controls in each look-back year (Figure 2)

• First observed occurrence of the cardiovascular conditions was often early in the 5-year look-back period prior to diagnosis of ATTRV

- Median time from first occurrence of a cardiovascular condition to diagnosis of ATTRv ranged from 15.4 months for patients with hypertrophic cardiomyopathy to 43.0 months for patients with chest pain (Figure 3) - Many of the cardiovascular conditions start to appear multiple (e.g., 3-5) years before a diagnosis of ATTRv, with dyspnea and chest pain most common throughout this period. Manifestation of certain conditions, such as bleeding, congestive heart failure, and hypotension became more frequent in the year prior to diagnosis (**Figure 4**)

• First observed occurrence of diagnostic testing such as cardiac MRI, echocardiogram, and blood-urine testing was also common several years before an ATTRv diagnosis; pyrophosphate imaging did not occur until the year before diagnosis among

• Hospitalization (47.5 vs. 24.3%), ED visits (60.3 vs. 47.0%) as well as cardiac imaging (56.7 vs. 27.0%) were more frequent among patients with ATTRv during the look-back period compared with matched controls (results not shown) - Echocardiography was the most common form of imaging performed in patients with ATTRv (56.7%), followed by cardiac magnetic resonance imaging (7.1%), and pyrophosphate imaging (2.1%) (results not shown)

\*Includes ischemic and hemorrhagic stroke

• Patients diagnosed with ATTRv amyloidosis have considerable cardiovascular burden in the 5 years preceding diagnosis • Increased awareness of characteristic cardiovascular manifestations may increase clinical suspicion, leading to early diagnosis and prompt intervention

- As the look-back period was only 5 years prior to diagnosis, pre-existing conditions (and other outcomes) may have been misclassified as first occurring during that period - Results may not be generalizable to patients without continuous enrollment in a healthcare plan or to those with other types of insurance coverage

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